(FILE 'HOME' ENTERED AT 11:38:08 ON 02 MAY 2003)

FILE 'MEDLINE, CANCERLIT, EMBASE, BIOSIS, CAPLUS, BIOTECHDS' ENTERED AT 11:38:26 ON 02 MAY 2003

L1	4372	S ANTIMICROBIAL PEPTIDE OR ANTIMICROBIAL POLYPEPTIDE OR ANTIMIC
L2	225564	S CATHETER OR STENT OR MEDICAL DEVICE
L3	10	S L2 AND L1
L4	9	DUP REM L3 (1 DUPLICATE REMOVED)
L5	726560	S GENE THERAPY OR (PLASMID OR VECTOR)
L6	306	S L5 AND L1
L7	28	S L6 AND GENE THERAPY
L8	21	DUP REM L7 (7 DUPLICATES REMOVED)

> d bib ab 1-9

L4 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2003 ACS
AN 2002:574969 CAPLUS
DN 137:129944
TI Implantable pulse generators composed of a polymer carrier and polynucleotides
IN Hendriks, Marc
PA Medtronic, Inc., USA
SO PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002058752	A2	20020801	WO 2001-US44435	20011127
	WO 2002058752	A3	20021121		
	WO 2002058752	C2	20030206		

RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR

PRAI US 2000-727461 A 20001204

AB The present invention relates to medical devices (e.g., implantable pulse generators) that include a polymer and a polynucleotide. Preferably, the **medical device** can be used to prevent or treat **medical device**-assocd. infections. In some aspects of the present invention, the medical devices carry a polynucleotide that encodes an **antimicrobial peptide** and inhibits the growth of pathogens. In other aspects of the present invention, the medical devices carry eukaryotic cells (e.g., endothelial cells) that express an **antimicrobial peptide** and inhibit the growth of pathogens.

L8 ANSWER 21 OF 21 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 5
AN 1996:661120 CAPLUS
DN 125:294754
TI Vectors carrying therapeutic genes encoding antimicrobial peptides for **gene therapy**
IN Guenzburg, Walter H.; Winder, David; Saller, Robert Michael
PA Bavarian Nordic, Den.; GSF-Forschungszentrum fuer Umwelt und Gesundheit GmbH
SO PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9628563	A1	19960919	WO 1996-EP1001	19960308
	W: AL, AM, AU, AZ, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9651039	A1	19961002	AU 1996-51039	19960308
	EP 817858	A1	19980114	EP 1996-907398	19960308
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI				
	JP 11503305	T2	19990326	JP 1996-527259	19960308
PRAI	DK 1995-243		19950309		
	WO 1996-EP1001		19960308		

AB The present invention relates to retroviral vectors carrying sequences encoding naturally occurring, antimicrobial peptides or derivs. thereof for the treatment of mammalian tumors, viral infections such as HIV infection and bacterial and fungal infections. In particular the present invention relates to retroviral vectors which undergo promoter conversion (Procon vectors) carrying such sequences. Since these vectors also carry tumor or virus specific regulatory elements, the therapeutic **antimicrobial peptide** will be delivered and expressed only in relevant, affected cells and not in innocent bystander cells. The U3 region of murine leukemia virus-derived **vector** BAG was replaced with a mouse mammary tumor virus U3 region without the inverted repeats but contg. the promoter, a region conferring responsiveness to glucocorticoid hormones, and a region contg. an element directing expression to the mammary gland. A preprocecropin A gene was inserted next to the promoter to produce **vector** p125.CercA. EJ cells expressing the luciferase gene fused to the HIV LTR and the Tat gene displayed luciferase expression. When these recombinant cells were infected with p125.CercA there was little luciferase expression.

L8 ANSWER 19 OF 21 MEDLINE DUPLICATE 4
AN 1998153409 MEDLINE
DN 98153409 PubMed ID: 9492532
TI Alteration of genomic structure and/or expression of cancer associated genes in hepatocellular carcinoma.
AU Fujimoto Y; Kohgo Y
CS Third Department of Internal Medicine, Asahikawa Medical College.
SO RINSHO BYORI. JAPANESE JOURNAL OF CLINICAL PATHOLOGY, (1998 Jan) 46 (1) 9-14. Ref: 11
Journal code: 2984781R. ISSN: 0047-1860.
CY Japan
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA Japanese
FS Priority Journals
EM 199804
ED Entered STN: 19980507
Last Updated on STN: 19980507
Entered Medline: 19980429
AB Cancer is thought to arise from the accumulation of several genetic mutations in a single cell. These include integration of viral genomes, activation of protooncogenes and inactivation of tumor suppressor genes. HCC is one of the most common cancers in Asia and Africa. Various studies have revealed its association with hepatitis B or C viral infection. While activation of known protooncogenes, such as ras genes does not seem to play an important role, frequent allelic loss on specific chromosomal arms, 4q, 13q, 16q and 17p, indicates that dysfunction of diverse tumor suppressor genes located on these chromosome arms is involved in the development of HCC. An informative p53 mutational spectrum of frequent G to T transversions in codon 249 is found in HCCs from either Qidong, People's Republic of China, or southern Africa. This observation links exposure to aflatoxin B1, a known cancer risk factor in these geographic regions. Recently, we found that expression of syndecan-1, which is a transmembrane heparan sulfate proteoglycan involved in cell matrix interactions and growth factor bindings, was inversely associated with metastatic potential in human hepatocellular carcinoma as like nm23-H1 expression was. Transfection with syndecan-1 gene suppresses invasive activity of hepatoma cells. These data support our hypothesis that syndecan-1 is one of important metastasis suppressor factors in hepatoma cells. PR-39 is a proline-rich **antimicrobial peptide** which was isolated from a pig small intestine and has been reported to induced syndecan-1 on mouse mesenchymal cells. Transfection with PR-39 gene caused induction of syndecan-1 and altered invasive phenotype and actin structure on hepatoma cells. Syndecan-1 and PR-39 may serve as a basis for design of drug or **gene therapy** effective against metastasis of hepatocellular carcinomas.

L8 ANSWER 18 OF 21 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 3
AN 1998:121274 BIOSIS
DN PREV199800121274
TI Expression of antimicrobial peptides has an antitumour effect in human cells.
AU Winder, David (1); Guenzburg, Walter H.; Erfle, Volker; Salmons, Brian (1)
CS (1) Bavarian Nordic Research Inst., D-80807 Munich Germany
SO Biochemical and Biophysical Research Communications, (Jan. 26, 1998) Vol. 242, No. 3, pp. 608-612.
ISSN: 0006-291X.
DT Article
LA English
AB The antimicrobial peptides cecropin and melittin are known to exhibit antitumour activity in tumour derived cell lines. To achieve a similar effect in vivo these peptides would have to be given repeatedly to maintain therapeutic levels, which may be pharmacologically unfavourable. The expression of the genes encoding such antimicrobial peptides in the desired cell type may circumvent these problems. Expression constructs carrying cecropin or melittin have been introduced into a human bladder carcinoma derived cell line and the resultant cell clones analysed for tumorigenicity in nude mice. Expression of cecropin resulted in either a complete loss of tumorigenicity in some clones or reduced tumorigenicity, as measured by latency of tumour formation. These results suggest that **vector** mediated delivery of this gene to tumour cells may prove useful for cancer **gene therapy**.

L8 ANSWER 15 OF 21 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT AND ISI
AN 1999-14674 BIOTECHDS
TI An antitumor agent;
plasmid pRC/CMV-mediated magainin, defensin, bactenecin, FALL39 and PR-39 gene transfer and expression in human hepatoma cell, used for **gene therapy**
PA Toray
LO Japan.
PI JP 11225762 24 Aug 1999
AI JP 1998-28922 10 Feb 1998
PRAI JP 1998-28922 10 Feb 1998
DT Patent
LA Japanese
OS WPI: 1999-521078 [44]
AB An antitumor agent composed of an effective ingredient of an **antimicrobial peptide** gene, particularly cathelin or defensin family peptide gene, especially PR-39 peptide gene derived from polynuclear leukocyte in pig skin lesion or small intestine is new. Also claimed are: an antitumor agent composed of a **vector** particularly **plasmid** pRC/CMV with an integrated **antimicrobial peptide** gene. Genes encoding for endogenous antimicrobial peptides include magainin from the skin of Xenopus sp., defensin from mammalian granulocytes and neutrophils including bactenecin derived from cattle neutrophils and FALL39-derived from human myeloid cells. Transduction of an **antimicrobial peptide** gene in tumor cells inhibits the infiltration activity of tumor cells, induces morphological changes of cells, decomposes actin-filament structure and leads to the inhibition of tumor metastasis. In an example, **plasmid** pRc/CMV was used for expression of syndecan-1 and PR-39 genes in human hepatoma cells. (12pp)

L8 ANSWER 14 OF 21 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 2
AN 1999:819489 CAPLUS
DN 132:74534
TI Methods of expressing anti-microbial proteins (especially lysostaphin) in specific cells/tissues, and uses thereof for the treatment of microbial infections such as mastitis
IN Bramley, John A.; Plaut, Karen I.; Kerr, David
PA University of Vermont and State Agricultural College, USA
SO PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9967381	A1	19991229	WO 1999-US14073	19990622
	W: AU, CA, JP, NZ				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	AU 9947067	A1	20000110	AU 1999-47067	19990622
	US 2002194629	A1	20021219	US 2002-87667	20020228
PRAI	US 1998-90175P	P	19980622		
	US 1999-337079	A	19990621		
	WO 1999-US14073	W	19990622		

AB The present invention relates to an improved approach for the treatment of microbial infections in mammals. Specifically, the invention provides methods and reagents for expressing in mammalian cells proteins that have anti-microbial activity. The invention provides both genes which have been modified to allow expression and preferably secretion of active protein in desired mammalian cells or tissues, and methods of introducing such modified genes into desired mammalian cells and/or tissues. In certain embodiments, the genes encoding anti-microbial proteins could include .beta.-lytic protease, -lytic protease, lyt-M, atlALE-1, and zooA, but the preferred gene encodes lysostaphin. Most specifically, genes encoding anti-staphylococcal proteins are delivered to mammalian cells and/or tissues, esp. mammary tissue, by methods of gene delivery, including **gene therapy** and the prodn. of transgenic animals, for the treatment of mastitis in ruminant animals.

L8 ANSWER 8 OF 21 MEDLINE DUPLICATE 1
AN 2002728302 IN-PROCESS
DN 22378701 PubMed ID: 12489997
TI A Model for Antimicrobial **Gene Therapy**: Demonstration of Human beta-Defensin 2 Antimicrobial Activities In Vivo.
AU Huang George T-J; Zhang Hai-Bo; Kim Daniel; Liu Lide; Ganz Tomas
CS Division of Associated Clinical Specialties, Section of Endodontics, UCLA School of Dentistry, Los Angeles, CA 90095.
SO HUMAN GENE THERAPY, (2002 Nov 20) 13 (17) 2017-25.
Journal code: 9008950. ISSN: 1043-0342.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS IN-PROCESS; NONINDEXED; Priority Journals
ED Entered STN: 20021220
Last Updated on STN: 20021220
AB We transfected host cells with an **antimicrobial peptide** /protein-encoding gene as a way to enhance host defense mechanisms against infection. The human beta-defensin 2 (HBD-2) gene was chosen as a model because its protein does not require cell type-specific processing. Using a retroviral **vector** carrying HBD-2 cDNA, we treated several mouse or human cell lines and primary cell cultures including fibroblasts, salivary gland cells, endothelial cells, and T cells. All transduced cells produced detectable HBD-2. In Escherichia coli gel overlay experiments, secreted HBD-2 from selected cell lines showed potent antimicrobial activity electrophoretically identical to that of purified HBD-2. We then used a mouse model (nonobese diabetic/severely compromised immunodeficient [NOD/SCID]) to test HBD-2 antimicrobial activities in vivo. HT-1080 cells carrying HBD-2 or control **vector** were implanted subcutaneously into NOD/SCID mice to allow tumor formation. Escherichia coli was then injected into each tumor mass. Tumors were resected after 16 hr and homogenized for bacterial colony-forming unit analysis. Compared with control tumors, HBD-2-bearing tumors contained only 7.8 +/- 3.3% viable bacteria. On the basis of this demonstration of HBD-2 in vivo antimicrobial activity, enhancement of antibacterial host defense by HBD-2 **gene therapy** may be feasible.

the treatment of mastitis in ruminant animals.

L8 ANSWER 2 OF 21 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT AND ISI
AN 2003-08552 BIOTECHDS
TI New DNA construct comprising a DNA sequence encoding an anti-microbial polypeptide, useful as veterinarian or human therapeutic or prophylactic agent for treating or preventing bacterial or fungal infection; **vector**-mediated recombinant protein gene transfer and expression in host cell for use in **gene therapy**
AU HANSEN M T
PA NOVOZYMES AS
PI WO 2002090384 14 Nov 2002
AI WO 2002-DK289 3 May 2002
PRAI DK 2001-706 4 May 2001; DK 2001-706 4 May 2001
DT Patent
LA English
OS WPI: 2003-111956 [10]
AB DERWENT ABSTRACT:
NOVELTY - A DNA construct comprising a DNA sequence encoding an anti-microbial polypeptide and consisting of: (a) a DNA sequence having 550 bp; or (b) a DNA sequence that is at least 60% identical to the part of (a) encoding the mature **antimicrobial peptide** or its fragment, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) a polypeptide exhibiting anti-microbial activity and encoded by the DNA sequence; (2) a recombinant expression **vector** comprising the DNA construct; (3) a cell comprising the DNA construct or the **vector**; (4) producing an anti-microbial polypeptide; or (5) an anti-microbial composition comprising the anti-microbial polypeptide.

BIOTECHNOLOGY - Preferred DNA: The DNA sequence is a cDNA, genomic DNA, synthetic DNA or mixed cDNA, or genomic and/or synthetic DNA sequence. It is derived from a filamentous fungus of the genus Aspergillus, in particular Aspergillus nigri or Aspergillus flavus. Preferred Polypeptide: The polypeptide is obtainable from a microorganism, preferably a bacterium or fungus, especially a filamentous fungus. The polypeptide comprises: (i) a 92-amino acid sequence (positions 1-58); or (ii) a fragment and/or variant of the 92-amino acid sequence (positions 1-58) exhibiting anti-microbial activity; or (iii) a fragment and/or variant as defined in (ii) that further has an N-terminal extension in comparison to the mature part of 92-amino acid sequence (positions 1-58). The anti-microbial peptide has a N-terminal extension of 1-50, 2-20 or preferably 3-15 amino acids. The N-terminal extension comprises a kex2 or kex2-like cleavage site and is a peptide, comprising at least two E and/or D amino acid residues. The N-terminal peptide does not contain an Arg (R). Preferred Cell: The cell is a bacterial or fungal cell. The bacterial cell is a cell of a gram-positive bacterium such as Bacillus or Streptomyces. The fungal cell is a yeast cell or a cell of Aspergillus, in particular of the species Aspergillus oryzae or Aspergillus niger. Preferred Composition: The anti-microbial composition further comprises an additional biocidal agent. Preferred Method: Producing an anti-microbial polypeptide comprises: (a) inserting a DNA construct encoding the anti-microbial polypeptide into a suitable expression **vector**; (b) transforming a suitable host cell with the recombinant expression **vector** of (a); (c) culturing the transformed host cell in a suitable culture medium for production of the anti-microbial polypeptide; and (d) recovering the anti-microbial polypeptide from the host cell or culture medium obtained in (c). The method further comprises modifying the polypeptide or its variant.

ACTIVITY - Fungicide; Antibacterial. No biological data given.

MECHANISM OF ACTION - **Gene therapy**.

USE - The anti-microbial polypeptide is useful as veterinarian or human therapeutic or prophylactic agent for treating or preventing

bacterial or fungal infection (claimed). (45 pages)

CLASS 604 Subclass Definition 890.1

CONTROLLED RELEASE THERAPEUTIC DEVICE OR SYSTEM:

Subject matter under the class definition in which the body is treated by a therapeutic delivery device or system which has dynamic structural means therein to controllably dispense a body treating material to the body over a prolonged period of time by the slow release of the said body treating material.

(1) **Note.** The delivery device may act to dispense the therapeutic means either continuously or discontinuously.

(2) **Note.** This and the indented subclass 890.1 provides for a device or system comprising a reservoir and control, pump or controllable valve means for dispensing a drug to a living body, in other words, a device which is more than a passive reservoir that is implanted or attached to the living body.

(3) **Note.** The devices of this and the indented subclasses contain moving mechanical parts which effect the release of drugs in a controlled manner.

SEARCH CLASS:

424, Drug, Bio-Affecting and Body Treating Composition, subclasses 422+ for preparations characterized by special physical form which release medication at a controlled rate where the inserted or implanted article is no more than (a) a single or multilayered assembly impregnated with or (b) a reservoir from which medicament is released by diffusion or osmosis; sublcass 448 for a bandage or transdermal or medicator held in place by a claimed pressure sensitive adhesive; subclass 449 for a transdemal or percutaneons device for the controlled release or medicament through the unbroken skin. Subclass 473 for a tablet with a porous perforated apertured or sieved layer for the controlled release of medicament; subclass 484 for an elutable or dissolvable matrix.

CLASS 607 Subclass Definition 36

Feature of stimulator housing or encapsulation: Subject matter under subclass 9 wherein significance is attributed to the material, construction, shape, etc. of either a container for the generator or a material encapsulating or filling the container.

SEARCH THIS CLASS, SUBCLASS :

9, for subject matter relating to the construction of the circuit, per se; e.g., chip architecture, component mounting, etc.